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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
ZEMAN, ROBERT A	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/686,529
Filing Date: October 16, 2003
Appellant(s): HELLINGA ET AL.

Gary R. Tanigawa
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 25 September 2011 appealing from the Office action mailed 14 September 2011.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Appellant appealed the final rejections in the divisional application 11/785,591.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-2, 7-15, 31-32 and 38-40 are pending and were finally rejected in the Office action mailed on 9-14-2011.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except

for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

U.S. Patent 6,277,627

U.S. Patent 6,855,556

U.S. Patent Application Publication U.S. 2003/0134346

WO 99/34212

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Issue One - Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 7-15, 31-32 and 38-40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,277,627.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims sets are drawn to biosensors comprising a bPGP and a reporter group wherein said reporter group is attached to the GBP and can constitute a fluorophore or a redox cofactor. Moreover, since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors.

Issue Two – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention.

Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The instant claims are drawn to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein

However, since no baseline sequence is provided for of the "glucose binding protein" and multiple glucose binding proteins (with differing sequences) are known in the art, none of these biosensor meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Moreover, the skilled artisan cannot envision the detailed chemical structure of the encompassed biosensors, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:
...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Given that there is no disclosed correlation between the structure (sequence) of the claimed biosensor and its claimed function (an alteration in the signaling of the reporter group of said biosensor due to the binding of glucose in a glucose-binding pocket of said biosensor) the requirements of proper description have not been met.

Issue Three - Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of term "...position 183 of said GBP...".Given that there is no base sequence recited in the claim and there are multiple sequences for GBP known in the art at the time of filing of the instant application, it is impossible to determine what specific amino acid is being claimed.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of phrase "...positions of said GBP selected from the group consisting of 10, 93 and 183.".

Given that there is no base sequence recited in the claim and there are multiple sequences for GBP known in the art at the time of filing of the instant application, it is impossible to determine what specific amino acid is being claimed.

Issue Four – Obviousness

First Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's statement regarding a possible declaration and request for an interview to discuss the evidence secondary factors favoring patentability of the claimed invention is noted. However, to date no declaration or secondary evidence has been made of record. Hence, any interview would be premature. Said evidence will be evaluated (and discussed with Applicant), if and when it is timely filed.

Claims 1-2, 7-15, 31-32 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (WO 99/34212 – IDS filed 3-14-2005).

Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see page 7, lines 18-19) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see page 8 lines 3-7 and claims 4-5). Hellinga also discloses that said

reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify any other bPBP other than GBP. Moreover, they do not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

2nd Rejection

Claims 1-2, 7-15, 31-32 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (U.S. Patent 6,277,627 – IDS filed 3-14-2005).

Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein GBP said include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see column 1, lines 46-48) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see column 3, lines 48-52 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of

Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

3rd Rejection

Claims 1-2, 7-15 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US 2003/0134346).

Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see paragraph 0025) and that a variety of reporter groups can be used such as fluorophores (e.g. acrylodan - see paragraph [0031]) and redox cofactors (see paragraph [0032]). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein. (see paragraph 0034). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose

that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

4th Rejection

Claims 1-2, 7-15 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US Patent 6,855,556).

Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (column 3, lines 44-50). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see column 5, lines 1-7) and that a variety of reporter groups can be used such as and redox cofactors (see

column 6, lines 55-59). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein (see column 6 line 65 to column 7, line 8). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific ΔI_{std} or ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

(10) Response to Argument

Issue One – Double Patenting

Appellant argues:

1. There is no motivation given as to why the skilled artisan would have attached one or more reporter groups at positions 10, 93 or 183.

2. There is no expectation of success shown in the Office action that attaching at least one reporter group at **any** position within GBP would result in the claimed biosensor.

3. The Examiner has failed to explain why the present claims 27-28 and 33-34 which are encompassed by claim 4 of the cited patent were not rejected.

4. The Examiner did not explain why one of ordinary skill in the art would have found it obvious to modify claims 1-8 of the '627 patent to satisfy the functional requirements set forth in claims 11-14.

5. Claims 31-32 require that the reporter group is acrylodan. The examiner did not explain why one of ordinary skill in the art would have found it obvious to modify claims 1-8 of the '627 to utilize acrylodan.

Examiner Rebuts

With regard to Point 1 since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors. Moreover, the specification of U.S. Patent 6,277,627 specifically discloses that the reporter groups can be **within the ligand-binding pocket** (i.e. can be an endosteric site) [see column 4, lines 21-22]. Moreover, the patent's specification also discloses (via the Marvin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see column 5, line 59]. It should be noted that residue 183 resides within the ligand binding pocket.

With regard to Point 2, while Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see

column 4 lines 21-48). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Additionally, given the success of Hellinga attaching a reporter group, both within and outside of the binding sites (see Examples 1 and 2); the skilled artisan would have had a reasonable expectation of success. Moreover, the patent's specification also discloses (via the Martin et al. reference) the means of selecting positions for reporter groups (fluorophores) [see column 5, line 59].

With regard to Point 3, claims 27-28 and 33-34 are not included in the rejection as they have been canceled.

With regard to Point 4, the biosensor with a reporter group at position 183, which is encompassed by the Hellinga patent in light of KSR, would necessarily have the same biochemical properties as that of the instant invention. Appellant is reminded the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. *In re* Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification of the biochemical properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir.1991). See M.P.E.P. 2145.

With regard to Point 5, the cited patent explicitly discloses the use of acrylodan as the reporter fluorophore (see Example 3 for example). Consequently, the use of acrylodan is clearly encompassed by the patented claims.

Issue Two – Written Description

Appellant argues:

1. This rejection contradicts the PTO's previous determination that the claims of Patent 6,277,627 satisfy all requirements for patentability.

2. U.S. Patent 6,277,627 was cited in the instant specification as describing *E. coli* periplasmic binding proteins including the glucose binding protein (GBP).

3. The sequences of GBP from other bacteria were also known in the prior art.

4. One of skill in the art would be able to align different GBP and identify a position corresponding to positions 10, 93 and 183 of the *E. coli* GBP.

Examiner Rebuts:

With regard to Point 1, although the Examiner's action in another application may appear to be inconsistent with the instant application, each case must stand on its own merits. In re Giolito and Hoffman 188 USPQ 645 (CCPA).

With regard to Points 2 and 3, the instant claims are not limited to bacterial (*E. coli*) GBPs.

With regard to Point 4, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid

itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Issue Three – Indefiniteness

Appellant argues:

1. The term "position" refers to the amino acid sequence of the bPBP.

2. The base sequence is the GBP amino acid sequence incorporated by reference from U.S. Patent 6,277,627.

3. No specific reference to a sequence is required because the GBPs are known in the art and numbering of their positions is known in the art.

Examiner Rebuts:

With regard to Points 1 and 3, the instant claims are not limited to *E. coli* GBPs. Moreover, because the sequence of bPBP is variable, skilled artisan would not know what the metes and bounds of the claimed invention were. The BLAST database demonstrates that there are over 100 different GBP sequences known in the art. Consequently, the residue identifiers (which are based on the *E. coli* GBP) have no correlation to a GBP for another species.

With regard to Point 2, there is no specific reference to said sequence in the rejected claim. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Issue Four – Obviousness Rejections

1st Rejection

Appellant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these **specific** positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. There is no technical or legal rationale provided by the Examiner why one of ordinary skill in the art would have attached a reporter group at the recited positions with a reasonable expectation of success.

4. The Examiner's reasoning is not acceptable to support a finding of *prima facie* obviousness as it merely invites one of ordinary skill in the art to experiment by attaching a reporter group at "any or all" positions of the amino sequence of a GBP. Thus, the Examiner's finding constitutes hindsight reasoning.

5. There is not a reasonable expectation of success to attach a reporter group to "any or all" positions within a GBP.

6. The Examiner was required to consider the claimed invention has decreased binding affinity to glucose and increased fluorescence characteristics.

7. The Examiner did not take into account the ΔI_{std} or ΔR_{max} values obtained by attaching a reporter group to position 183 which were experimentally determined by Applicant's.

8. The biosensors of Hellinga would not have the same biochemical properties as that of the instant invention as Hellinga does not disclose the attachment of the reporter groups to the recited amino acid positions.

9. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

10. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}\ \Delta R_{max}$ values.

Examiner Rebuts:

With regard to Points 1-3 and 5, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17). While Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Point 4), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so

long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Moreover, the KSR decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Given that Hellinga et al. disclose the attachment of the reporter group to multiple binding sites and that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket, the attachment to of a reporter site to a given position is well within the capabilities of one of ordinary skill in the art. Moreover, the disclosure of Hellinga sets forth a finite number of possible alternatives. Consequently, the requirements of obviousness under the KSR decision are met.

With regard to Point 6, only claims 11-14 recite any limitation regarding glucose binding affinity or fluorescence characteristics. Moreover, the biosensors resulting from the obvious modifications of the cited reference would necessarily possess the same biochemical characteristics as the biosensors of the instant invention.

With regard to Point 7, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. *In re* Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the obvious variation of the reference that would inherently lead to the modification of the biochemical properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious.

Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Points 8 and 10, the biosensor with a reporter group at position 10, 93 or 183, which is encompassed by Hellinga **in light of KSR**, would necessarily have the same biochemical properties as that of the instant invention. Moreover, the instant claims are not limited to *E. coli* GBPs.

With regard to Point 9, Hellinga discloses that the binding constant of GBP can be changed via site-directed mutagenesis (see page 11, line 14 to page 12, line14).

2nd Rejection

Appellant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these **specific** positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. There is no technical or legal rationale provided by the Examiner why one of ordinary skill in the art would have attached a reporter group at the recited positions with a reasonable expectation of success.

4. The Examiner's reasoning is not acceptable to support a finding of *prima facie* obviousness as it merely invites one of ordinary skill in the art to experiment by attaching a reporter group at

"any or all" positions of the amino sequence of a GBP. Thus, the Examiner's finding constitutes hindsight reasoning.

5. There is not a reasonable expectation of success to attach a reporter group to "any or all" positions within a GBP.

6. The Examiner was required to consider the claimed invention has decreased binding affinity to glucose and increased fluorescence characteristics.

7. The Examiner did not take into account the $\Delta I_{std\ or}$ ΔR_{max} values obtained by attaching a reporter group to position 183 which were experimentally determined by Applicant's.

8. The biosensors of Hellinga would not have the same biochemical properties as that of the instant invention as Hellinga does not disclose the attachment of the reporter groups to the recited amino acid positions.

9. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

10. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}$ ΔR_{max} values.

Examiner Rebuts:

With regard to Points 1-3 and 5, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17). While Hellinga does

not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Point 4), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Moreover, the KSR decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Given that Hellinga et al. disclose the attachment of the reporter group to multiple binding sites and that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket, the attachment to of a reporter site to a given position is well within the capabilities of one of ordinary skill in the art.

Moreover, the disclosure of Hellinga sets forth a finite number of possible alternatives. Consequently, the requirements of obviousness under the KSR decision are met.

With regard to Point 6, only claims 11-14 recite any limitation regarding glucose binding affinity or fluorescence characteristics. Moreover, the biosensors resulting from the obvious modifications of the cited reference would necessarily possess the same biochemical characteristics as the biosensors of the instant invention.

With regard to Point 7, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. *In re* Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the obvious variation of the reference that would inherently lead to the modification of the biochemical properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Points 8 and 10, the biosensor with a reporter group at position 10, 93 or 183, which is encompassed by Hellinga **in light of KSR**, would necessarily have the same biochemical properties as that of the instant invention. Moreover, the instant claims are not limited to *E. coli* GBPs.

With regard to Point 9, Hellinga discloses that the binding constant of GBP can be changed via site-directed mutagenesis (see column 5, lines 10-37).

3rd Rejection

Appellant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Amiss et al. disclose does not teach or suggest attaching at least one reporter group to these **specific** positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. There is no technical or legal rationale provided by the Examiner why one of ordinary skill in the art would have attached a reporter group at the recited positions with a reasonable expectation of success.

4. The Examiner's reasoning is not acceptable to support a finding of *prima facie* obviousness as it merely invites one of ordinary skill in the art to experiment by attaching a reporter group at "any or all" positions of the amino sequence of a GBP. Thus, the Examiner's finding constitutes hindsight reasoning.

5. There is not a reasonable expectation of success to attach a reporter group to "any or all" positions within a GBP.

6. The Examiner was required to consider the claimed invention has decreased binding affinity to glucose and increased fluorescence characteristics.

7. The Examiner did not take into account the $\Delta I_{std\ or}$ ΔR_{max} values obtained by attaching a reporter group to position 183 which were experimentally determined by Applicant's.

8. The biosensors of Amiss et al. would not have the same biochemical properties as that of the instant invention as Amiss et al. does not disclose the attachment of the reporter groups to the recited amino acid positions.

9. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

10. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same ΔI_{std} or ΔR_{max} values.

Examiner Rebuts:

With regard to Points 1-3 and 5, , Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss further discloses does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss et al. attaching a reporter group both within and outside of the binding sites (see Examples), the skilled artisan would have had a reasonable expectation of success.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Point 4), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so

long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Moreover, the KSR decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Given that Amiss et al. disclose the attachment of the reporter group to multiple binding sites and that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket, the attachment to of a reporter site to a given position is well within the capabilities of one of ordinary skill in the art. Moreover, the disclosure of Amiss et al. sets forth a finite number of possible alternatives. Consequently, the requirements of obviousness under the KSR decision are met.

With regard to Point 6, only claims 11-14 recite any limitation regarding glucose binding affinity or fluorescence characteristics. Moreover, the biosensors resulting from the obvious modifications of the cited reference would necessarily possess the same biochemical characteristics as the biosensors of the instant invention.

With regard to Point 7, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. *In re* Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the obvious variation of the reference that would inherently lead to the modification of the biochemical properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious.

Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Points 8 and 10, the biosensor with a reporter group at position 10, 93 or 183, which is encompassed by Amiss et al. **in light of KSR**, would necessarily have the same biochemical properties as that of the instant invention. Moreover, the instant claims are not limited to *E. coli* GBPs.

With regard to Point 9, Amiss et al. discloses that the binding constant of GBP can be changed via site-directed mutagenesis (see column 5, lines 50-56).

4th Rejection

Appellant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Amiss et al. disclose does not teach or suggest attaching at least one reporter group to these **specific** positions and there is no reason provided why one of ordinary skill in the art would have attached one or more reporter groups at these specific positions.

3. There is no technical or legal rationale provided by the Examiner why one of ordinary skill in the art would have attached a reporter group at the recited positions with a reasonable expectation of success.

4. The Examiner's reasoning is not acceptable to support a finding of *prima facie* obviousness as it merely invites one of ordinary skill in the art to experiment by attaching a reporter group at

"any or all" positions of the amino sequence of a GBP. Thus, the Examiner's finding constitutes hindsight reasoning.

5. There is not a reasonable expectation of success to attach a reporter group to "any or all" positions within a GBP.

6. The Examiner was required to consider the claimed invention has decreased binding affinity to glucose and increased fluorescence characteristics.

7. The Examiner did not take into account the $\Delta I_{std\ or}\ \Delta R_{max}$ values obtained by attaching a reporter group to position 183 which were experimentally determined by Applicant's.

8. The biosensors of Amiss et al. would not have the same biochemical properties as that of the instant invention as Amiss et al. does not disclose the attachment of the reporter groups to the recited amino acid positions.

9. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

10. The biosensors disclosed in the reference are different as compared to the claimed biosensors and would not have the same $\Delta I_{std\ or}\ \Delta R_{max}$ values.

Examiner Rebuts:

With regard to Points 1-3 and 5, Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss further discloses does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of

reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss et al. attaching a reporter group both within and outside of the binding sites (see Examples), the skilled artisan would have had a reasonable expectation of success.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning (Point 4), it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Moreover, the KSR decision sets forth "if a technique has been used to improve one device, and a person of skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond that person's skill". Given that Amiss et al. disclose the attachment of the reporter group to multiple binding sites and that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket, the attachment to of a reporter site to a given position is well within the capabilities of one of ordinary skill in the art. Moreover, the disclosure of Amiss et al. sets forth a finite number of possible alternatives. Consequently, the requirements of obviousness under the KSR decision are met.

With regard to Point 6, only claims 11-14 recite any limitation regarding glucose binding affinity or fluorescence characteristics. Moreover, the biosensors resulting from the obvious

modifications of the cited reference would necessarily possess the same biochemical characteristics as the biosensors of the instant invention.

With regard to Point 7, the mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. *In re* Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the obvious variation of the reference that would inherently lead to the modification of the biochemical properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

With regard to Points 8 and 10, the biosensor with a reporter group at position 10, 93 or 183, which is encompassed by Amiss et al. **in light of KSR**, would necessarily have the same biochemical properties as that of the instant invention. Moreover, the instant claims are not limited to *E. coli* GBPs.

With regard to Point 9, Amiss et al. discloses that the binding constant of GBP can be changed via site-directed mutagenesis (see column 5, lines 50-56).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/ROBERT A ZEMAN/
Primary Examiner, Art Unit 1645
December 1, 2011

Conferees:

/Gerald G. Leffers Jr./
Primary Examiner 1600
December 1, 2011

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1645